

DOCKET NO.: PUJ-0279
Applicati n No.: 09/634,399
Office Acti n Dated: April 11, 2003

REMARKS

Claims 1, 3-23, 25-30, 33-36, 38-41, 43-55, 57-62, 64-89, 91-101, 103, 104, and 111-118 are currently pending and stand rejected. Claims 1, 22, 36, 50, 53, 57-60, 62, and 79 are amended herein. Claims 42, 56, and 90 have been canceled and incorporated into Claims 1, 36, and 79, respectively. Although the application is under a final rejection, Applicants respectfully request entry of these amendments under 37 C.F.R. § 1.116, as the amendments merely clarify the meaning of certain terms that were present in the claims previously, and present no new issues that would require an additional search.

Rejection under Section 102(b)

Claims 79 to 83, 85, 86, 90 to 101, 104, 117 and 118 stand rejected under 35 U.S.C. § 102(b) over Grollier, et al., GB 2194887.

As amended herein, independent Claim 79 is directed to a non-gelled composition that consists essentially of minoxidil, a thickening agent, and at least about 20% of a pharmaceutically acceptable solvent, wherein the solvent is *selected from the group consisting of an alcohol and a polyol*. Additionally, Claim 79 requires that the minoxidil must be present in a concentration which *is less than its solubility limit in said composition*, and that the composition is not in the form of an oil-in-water emulsion.

The amendments to Claim 79 have been made to clarify the meaning of certain terms that were present in the claims previously. Specifically, the term “substantially solubilized” has been removed from the claim, and replaced with the definition of the term from the specification (*see page 6, lines 15-17*). Additionally, amended Claim 79 requires at least about 20% of a solvent selected from the group consisting of an alcohol and a polyol. Thus, the claim requires at least about 20% of a solvent *other than water*. Applicants respectfully

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submit that one of skill in the art would have understood that the term “pharmaceutically acceptable solvent,” as used throughout the application, was not intended to include water (since minoxidil will not dissolve in water, to any appreciable extent). However, by amending the claim, this requirement is now explicit.

It is clear that Grollier does not anticipate Claim 79. Contrary to the requirements of the claim, Grollier specifies that the minoxidil is present in the compositions in an amount *greater than its solubility limit*. See Grollier page 2, lines 25-27. Thus, Grollier clearly *teaches away* from the compositions of the present invention. Moreover, Grollier fails to teach or suggest any compositions that contain at least about 20% of a solvent selected from the group consisting of an alcohol and a polyol. In examples 1-3 of Grollier, the solvents listed are 2-butoxyethanol, ethyl alcohol, and propylene glycol. In examples 6-12, and 15, the solvents include ethanol, propylene glycol, and dipropyleneglycol methyl ether. In each of these examples, the solvents are present in amounts of less than 20%. In fact, Grollier expressly prefers less than 20% of solvent with 1-10% solvent being more preferred. See Grollier page 2, lines 35-36.

As discussed in the instant application, one of skill in the art would appreciate that it is difficult to produce pharmaceutically elegant, thickened preparations of minoxidil, in which the minoxidil does not precipitate out of solution upon the addition of thickening agents, particularly when using higher concentrations of minoxidil. Previous attempts to produce such preparations have been hindered by processing difficulties due to the poor solubility of minoxidil. High percentages of solvents may be used to dissolve the minoxidil but these compositions have led to thick, doughy masses that are unusable as

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pharmaceutically elegant preparations. Compositions as defined, for example in claim 79, overcome these prior art difficulties.

Since Grollier fails to teach each and every element of Claim 79, Applicants respectfully request that the rejection of that claim and all the claims dependent thereon under Section 102 be withdrawn.

Rejections under Section 103(a)

Claims 79 to 83, 85, 86, 90 to 101, 104, 117 and 118 stand rejected under 35 U.S.C. § 103 over Grollier, further in view of Sine et al (U.S. Patent No. 6,423,329) and Preuilh et al (U.S. Patent No. 6,106,848). Applicants respectfully submit that any proper combination of these references fails to teach or suggest the composition defined by Claim 79.

As noted above, Grollier *teaches away* from compositions in which the minoxidil is present in an amount greater than its solubility limit. Grollier also fails to teach or suggest compositions that contain at least about 20% of a solvent selected from the group consisting of an alcohol and a polyol. Indeed, Grollier *teaches away* from the use of these higher concentrations of solvent. Thus, any proper combination with Sine and/or Preuilh will not result in the composition defined by Claim 79, as Grollier's explicit teaching away from the compositions defined by Applicants' claims cannot be ignored.

Moreover, Claim 79 requires that the composition is not in the form of an oil-in-water emulsion. As noted in the Office Action (*see* page 9), Preuilh is specifically directed to oil-in-water emulsions, and thus also *teaches away* from the composition defined by Claim 79. Thus, there is nothing in either Grollier or Preuilh that would provide any motivation to prepare a composition as defined by this claim.

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Additionally, as Applicants have pointed out in previous responses, Sine does not teach a single composition that contains minoxidil. Thus, there is nothing in this reference that would lead one of ordinary skill in the art to conclude that the use of an acrylate/C₁₀₋₃₀ alkyl acrylate crosspolymer would succeed in producing a minoxidil composition in which the minoxidil *would remain solubilized*, particularly in view of the fact that Grollier *teaches away* from such compositions.

Thus, Applicants respectfully submit that any proper combination of Grollier, Sine and/or Preuilh fails to teach or suggest the composition defined by Claim 79 as amended herein, and hence the claims dependent thereon. Accordingly, Applicants respectfully request that the rejection of Claims 79 to 83, 85, 86, 90 to 101, 104, 117 and 118 under 35 U.S.C. § 103 be withdrawn.

In the Office Action dated April 11, 2003, Claims 1, 3 to 7, 11 to 14, 17, 18, 21 to 23, 25, 26, 28 to 30, 33 to 35 and 111 stand rejected under Section 103 over Preuilh. Applicants respectfully submit that the previously pending claims define over Preuilh, for the reasons, for example, that were set forth in the response submitted February 20, 2003. Nonetheless, in the interest of advancing prosecution of this application, Applicants have amended Claim 1 to more clearly distinguish the claimed compositions from those described in Preuilh.

Claim 1 is directed to a composition that comprises minoxidil, a non-carbomeric organic thickening agent, and a pharmaceutically acceptable solvent, wherein the non-carbomeric thickening agents is other than hydroxypropyl cellulose. As amended herein, Claim 1 further requires that the composition be *in the form of a single-phase gel*, and said minoxidil is *present at a concentration which is less than its solubility limit*.

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As noted by the Examiner, Preuilh is directed to oil-in-water emulsions. Preuilh teaches, however, that the emulsions can contain a thickening or “gelling” agent. As set forth in the instant specification, emulsions are considered “non-gelled” compositions, within the lexicon of this application. Despite the fact that the application specifically distinguishes “gels,” as the term is used in this application, and emulsions, the Office Action states that this does not define over Preuilh, because it is known that emulsions can be in the form of gels (*see* Office Action, page 11). Applicants respectfully submit that they are permitted by the patent laws to be their own lexicographers, and that one of skill in the art, on the basis of the specification and prosecution to date, would understand that the claimed gels would not include the thickened oil-in-water emulsions described in Preuilh.

Those issues notwithstanding, one of ordinary skill in the art will readily understand that oil-in-water emulsions are two-phase (or multi-phase) systems. Thus, amended Claim 1, which specifies that the compositions are *single-phase gels*, clearly defines over Preuilh. Additionally, there is nothing in Preuilh that would lead one of ordinary skill in the art to prepare a single-phase gel of the present invention, because Preuilh is directed solely to multi-phase systems. Accordingly, Applicants respectfully request that the rejection of Claims 1, 3 to 7, 11 to 14, 17, 18, 21 to 23, 25, 26, 28 to 30, 33 to 35 and 111 over Preuilh be reconsidered and withdrawn.

Claims 8 to 10, 15, 16, 36, 38 to 52, 56 to 62, 64 to 70, 74 to 76, 78 and 112 to 116 stand rejected under Section 103 over Prueilh in view of Samour (U.S. Patent No. 5,620,980) and Sine. Applicants respectfully disagree that these references teach or suggest the subject matter of the previously pending claims. However, in the interest of advancing prosecution

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of these claims to allowance, Applicants have amended Claim 1, and thus dependent claims 7 to 10, 15, 16, and 111 to more clearly distinguish Preuilh, Samour and Sine. Applicants have also amended independent claims 36 and 62, and thus dependent claims 38 to 41, 43 to 55, 57 to 61, 64 to 78, and 113 to 116, to more clearly distinguish Preuilh, Samour and Sine.

Like Claim 1, discussed *supra*, Claims 36 and 62 have been amended to clarify that in the claimed compositions, the minoxidil is *present at a concentration which is less than its solubility limit*. These claims have also been amended to clarify that the compositions are in the form of a *single-phase gel*. Since any proper combination of Preuilh, Samour and Sine fail to teach or suggest the claimed compositions, Applicants respectfully submit that the references fail to establish the *prima facie* obviousness of the rejected claims.

As discussed above, Preuilh, the primary reference relied on by the Examiner, is directed solely to thickened oil-in-water emulsions that are, by definition, multi-phase systems. Thus, Preuilh *teaches away* from the single-phase gels defined by amended Claims 1, 36 and 62. It is stated in the Office Action that Preuilh lacks disclosure of alcohols as a solvent, solvent-tolerant carbomers as thickeners, and the preferred percentages of polyols, and Samour is relied on for these teachings. However, even if these elements are combined with the teachings of Preuilh, one is still left with *thickened multi-phase systems*, not the single-phase gels defined in the instant claims. Similarly, even if one of ordinary skill in the art were also to consult Sine (which Applicants do not concede one would be motivated to do), one would still understand only that additional thickeners could be used to thicken *multi-phase systems*. Thus, the addition of Samour and Sine to the basic teaching of Preuilh, a reference that *teaches away* from the instantly claimed compositions, cannot overcome the deficiencies of the primary reference, and any proper combination of these references fails to

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establish the *prima facie* obviousness of Applicants' amended claims. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 19, 20, and 53 to 55 stand rejected under Section 103 over Preuilh, in view of Anton et al (U.S. Patent No. 5,798,426) and Grollier. Applicants respectfully submit that this rejection fails, for reasons discussed above with regard to Preuilh and Grollier. Specifically, Preuilh does not teach single-phase gels, and Grollier requires that the minoxidil be present in a concentration that is greater than its solubility limit in the composition. Thus, both of these references *teach away* from the invention defined by these claims. The addition of Anton, and its teaching of amino methyl propanol, does nothing to overcome the deficiencies of the other two references. Accordingly, Applicants respectfully request that this rejection be withdrawn.

Claims 71 to 73 stand rejected under Section 103 over Preuilh in view of Samour and Sine, and further in view of Anton and Grollier. Applicants respectfully submit that this rejection fails for the same reasons that Preuilh, Samour and Sine fail to teach or suggest the composition of independent Claim 62, as discussed above. As also discussed with regard to Claims 19, 20 and 53 to 55, the addition of Anton and Grollier (which again, *teaches away* from the claimed invention) does nothing to overcome these deficiencies. Accordingly, Applicants respectfully request that this rejection be withdrawn

Claim 87 is rejected under Section 103 over Grollier, and further in view of Sine and Preuilh. As discussed above with regard to Claim 79 from which Claim 87 depends, Grollier

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teaches away from the claimed composition, in that it requires that the minoxidil be present at a concentration which is above its solubility limit. Prueilh also *teaches away* from the claimed compositions, in that it is directed to oil-in-water emulsions, which are specifically excluded from Claim 87. Thus, the addition of Sine's teaching can do nothing to overcome the deficiencies of the other two references, and the combined teachings fail to establish the *prima facie* obviousness of Claim 87. Accordingly, Applicants respectfully request that the rejection be withdrawn.

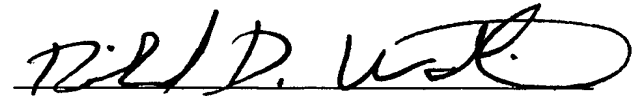
Claim 103 stands rejected under Section 103 over Grollier, further in view of Samour. As discussed above, Grollier, the primary reference in this rejection *teaches away* from the composition defined by Claim 79, in that it requires that the minoxidil be present in a concentration greater than its solubility limit. The combination with Samour fails to overcome this fundamental deficiency in the primary reference, and thus fails to establish the *prima facie* obviousness of Claim 103. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The foregoing represent a *bona fide* attempt to advance this case to allowance. There being no additional pending rejections that have not been addressed, Applicants respectfully submit that this application is now in condition for allowance. Accordingly, an indication of allowability and an early Notice of Allowance of all currently pending claims are respectfully requested.

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In the event that the Examiner is of a contrary view, the courtesy of a telephone call to Applicants' undersigned representative is respectfully requested.

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